

Annex to:

EFSA NDA Panel, 2022. Scientific Opinion on the Tolerable Upper Intake Level for dietary sugars. EFSA Journal 2022;20(2):7074. doi:10.2903/j.efsa.2022.7074

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1. Intervention studies on metabolic diseases

Publication	Exposure-endpoint excluded	Reasons for exclusion
Lowndes et al. (2014)	SSBs – Blood pressure	No results available in the publication for SBP and DBP per intervention arm. No response from the authors. Only this exposure-outcome pair was excluded from the assessment.
Majid et al. (2013)	SSBs – Body weight	Description of the method used to measure body weight and pre- and post-intervention results for body weight not reported. No response from the authors. Only this exposure-outcome pair was excluded from the assessment.
Mann et al. (1970)	Added sugars (sucrose) – triglycerides	Baseline consumption of sugar not reported for both intervention arms.
de Moraes et al. (2017)	SSBs – fasting glucose/total cholesterol	Baseline consumption of beverages not given for the full sample included in the analysis.
Silbernagel et al. (2011)	Fructose/Glucose – glucose and insulin concentrations at 120' during an OGTT	Values for glucose and insulin concentrations at 120' during the OGTT for the glucose and fructose intervention groups not reported in the publication. No response from the authors. Only these exposure-outcome pairs were excluded from the assessment.
Ebbeling et al. (2006)	SSBs – Body weight, BMI	This is a linked reference of another paper which reported on the same exposure-endpoints from which data was extracted for the assessment.
Katan et al. (2016)	SSBs – Body weight, waist circumference	This is a linked reference of another paper which reported on the same exposure-endpoints from which data was extracted for the assessment.
Yu et al. (2013)	SSBs – Fasting insulin, triglycerides	Results presented in a graph only from which data could not be extracted. This is a linked reference of another paper which reported on the same exposure-endpoint from which data was extracted for the assessment.
Reiser et al. (1989)	Fructose – Insulin, glucose	Only day-long postprandial glucose and insulin values were reported.
Poppitt et al. (2002)	Added sugars – Body weight, triglycerides, total cholesterol, HDL-c, LDL-c	This is a linked reference of another paper which reported on the same exposure-endpoints from which data was extracted for the assessment.
Stanhope et al. (2011)	Added sugars – Fasting insulin, fasting glucose	This is a linked reference of another paper which reported on the same exposure-endpoints from which data was extracted for the assessment.

BMI, body mass index; DBP, diastolic blood pressure; HDL-c, high density lipoprotein cholesterol; LDL-c, low density lipoprotein cholesterol; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; SSBs, sugar-sweetened beverages.



2. Observational studies on metabolic diseases

Cohort, publication	Exposure-endpoint excluded	Reasons for exclusion
ALSPAC Avon Longitudinal Study of Parents and Children	Dietary pattern z-scores – fat mass	Results only reported by dietary pattern z-scores and not for any of the exposures of interest as independent variables. Authors could not provide this information.
Ambrosini et al. (2016) BMES Blue Mountain Eyes Study	Total sugars – CVD	Unclear whether prevalent cases of CVD were excluded at baseline. No response from the authors.
Iff et al. (2014) BSCC Bogota School Children Cohort Charaff et al. (2014)	SSBs – BMI/WC/body fat	Population group were children aged 5-12 years. Anthropometric measurements were not standardised by age.
COSM Cohort of Swedish Men	Chocolate – Heart failure	Not on exposure of interest.
COSM Cohort of Swedish Men	SSBs – Heart failure	The exposure did not differentiate between artificially sweetened and sugar sweetened beverages.
Rahman et al. (2015) ECLS-BC Early Childhood Longitudinal Study – Birth cohort	FJs – Overweight/BMIz-scores	Exposure assessed by dietary interview alone.
Shefferly et al. (2016) EPIC-C3N European Prospective Investigation into Cancer and Nutrition- French cohort	SSBs / FJs – T2DM	The EPIC-InterAct (InterAct consortium, 2013) includes this French cohort for the same exposures and endpoint, and thus this paper was excluded to avoid duplication of cases.
EPIC-Morgen European Prospective Investigation into Cancer and Nutrition- Morgen cohort	Total sugars - CHD	This cohort was included in a bigger study found during the literature search update for the same exposure-endpoint pair. Only this exposure-outcome pair was excluded from the assessment.
Burger et al. (2011) EPIC-Norfolk European Prospective Investigation into Cancer and Nutrition- Norfolk cohort	Total sugars – T2DM	The EPIC-InterAct (Sluijs et al., 2013) includes this UK cohort for the same exposure and endpoint, and thus this paper was excluded (for this exposure-endpoint relationship only) to avoid duplication of cases.
Ahmadi-Abhari et al. (2014) EPIC-Norfolk European Prospective	Total sugars / total sucrose – Obesity	Prevalent cases of obesity not excluded at baseline. Only this exposure-outcome pair was
Investigation into Cancer and Nutrition- Norfolk cohort Kuhnle et al. (2015)	Obesity	excluded from the assessment.



EPIC-Norfolk European Prospective Investigation into Cancer and Nutrition- Norfolk cohort	SSBs / FJs – T2DM	The EPIC-InterAct (InterAct consortium, 2013) includes this UK cohort for the same exposures and endpoint, and thus this paper was excluded to avoid duplication of cases.
(O'Connor et al. 2015)		
(O'Connor et al., 2015) EPICOR European Prospective Investigation into Cancer and Nutrition- Italian cohort	Total sugars - CHD	This cohort was included in a bigger study found during the literature search update for the same exposure-endpoint pair.
Sieri et al. (2010)		
EPIC-Utrecht European Prospective Investigation into Cancer and Nutrition- Utrecht cohort	Total sugar - CHD	Exposure-endpoint pair on this cohort was included in a bigger study found during the search update. Only this exposure-outcome pair was excluded from the assessment.
Beulens et al. (2007)		
EYHS-DK European Youth Heart Study-Denmark cohort	Total sugars / sucrose / SSBs / FJs – BMIz-score /WC /body fat	Unclear if exposure assessment (24-h recall) covered single or multiple days. No response from the authors.
Olsen et al. (2012) Zheng et al. (2015)b Zheng et al. (2014)		
Fiorito et al. (2009)	SSBs – BMIz-score/WC/body fat	Standardised regression coefficients only (no absolute size of effect).
FMCHES Finnish Mobile Clinic Health Examination Survey	Glucose+Fructose – T2DM	Exposure not comparable with others in the assessment. Only this exposure-outcome pair was excluded from the assessment.
Montonen et al. (2007)		
Generation R Leermakers et al.	SSBs – Blood pressure, blood lipids	Intake per tertiles of sugar-sweetened beverages not reported and standardised regression coefficients only (no absolute size of
(2015) GUTS	FJs – BMI	effect).
Growing Up Today Study Berkey et al. (2004)	FJS — DIVII	Exposure-endpoint pair on this cohort was reported in another publication included in the assessment that reports on BMIz-scores which is a more appropriate measure for the population sample. Only this exposure-outcome pair was excluded from the assessment.
HPFS Health Professionals Follow-up Study	SSBs – CHD	This cohort was included in a bigger study found during the literature search update for the same exposure-endpoint pair.
de Koning et al. (2012)		
HPFS/NHS Health Professionals Follow-up Study/Nurses Health Study	Citrus fruit juice – ischemic CVD, ischemic stroke	Mean intakes of fruit juice at baseline not reported.
Joshipura et al. (2009)		
HPFS/NHS Health Professionals Follow-up Study/Nurses Health Study	SSBs – T2DM	The paper reports on caffeinated vs caffeine- free carbonated beverages. Another paper reporting on this exposure-endpoint for these cohort was identified.



Bhupathiraju et al.		T
(2013)		
HWP	SSBs – Body weight	Reports on weekly frequency of consumption
Healthy Worker Project		only.
French et al. (1994)		
MDCS	Dietary patterns – WC/Blood	Results only reported by dietary pattern z-scores
Malmo Diet Cancer	lipids/Blood pressure/Glucose	and not for any of the exposures of interest as
Study	homeostasis	independent variables.
Drake et al. (2019)		
Drake et al. (2018) NHS	FJs – T2DM	Exposure-endpoint pair was also identified in
Nurses Health Study	133 12511	another publication on this cohort which
,		reported on a longer follow-up time, and thus
Bazzano et al. (2008)		was included instead.
NHS	Sucrose – T2DM	Quantitative baseline mean intakes not reported.
Nurses Health Study		
Colditz et al. (1992)		
NHS	Sucrose/Fructose – CHD	Mean intakes, number of incident cases and
Nurses Health Study		person-years per energy-adjusted quintile of
Liu et al. (2000)		these nutrients were not reported. Authors could not provide the data prior to the closing of the
Liu et al. (2000)		database.
NHS	SSBs – CHD	This cohort was included in a bigger study found
Nurses Health Study		during the literature search update for the same
E (2000)		exposure-endpoint pair.
Fung et al. (2009) NHS	T2DM	Results only reported according to family history
Nurses Health Study	I ZDM	of T2DM and not for any of the exposures of
Traises Fledial Stady		interest as independent variables.
van 't Riet et al. (2010)		·
Northampton	Total sugars – Birthweight	Unclear analysis and absolute values for the
Langley-Evans and		analysis of sugar intake during pregnancy and neonate birthweight not reported. Authors could
Langley-Evans (2003)		not provide this information.
WEC	Sucrose – CHD	Retrospective analysis.
Western Electric		
Company		
Paul et al. (1968)		
PURE-South Africa	Added sugars – BMI/WC/HDL-	Retrospective analysis.
Prospective Urban and	c	,
Rural Epidemiology –		
South Africa cohort		
Vorster et al. (2014)		
QNTS	SSBs/ FJs – BMI	Correlation coefficients only (no absolute size of
Quebec Newborn Twin		effect).
Study		
Dubois et al. (2016)		
Skinner and Carruth	FJs – Body weight/BMI	Average intake over the follow-up not reported
(2001)	, , ,	and authors contact details not retrievable.
SMC	Chocolate – Stroke	Not on exposure of interest.
Swedish Mammography Cohort		
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Conorc		
Larsson et al. (2011)		
Larsson et al. (2011)	SSBs – Abdominal obesity,	Analysis not eligible (change in exposure vs
Larsson et al. (2011)	SSBs – Abdominal obesity, HTN, high HDL-c, high TG, High FPG	Analysis not eligible (change in exposure vs incident endpoint at the time of the last exposure assessment). Only these exposure-



Barrio-Lopez et al. (2013)		outcome pairs were excluded from the assessment.
TLGS Teheran Lipid and Glucose Study Hosseini Esfahani et al. (2014)	Added sugars — Body weight	Results for body weight presented as dichotomous endpoints, "weight gain" or "weight loss", and exposure per "increased intake" or "decreased intake". Not comparable with any other studies.
UK Biobank Ho et al. (2020)	Total sugars – CVD	Exposure estimated from the average of five assessments and 37% of participants had only completed one of five dietary questionnaires.
VITAL The Vitamins and Lifestyle study Barrington and White (2016)	SSBs – CVD	Prevalent cases of CVD not excluded at baseline.
WAPCS Western Australia Pregnancy Cohort (Reine) Study Ambrosini et al. (2013)	SSBs – Obesity	Authors confirmed prevalent cases of overweight/obesity at baseline were not excluded. Only this exposure-outcome pair was excluded from the assessment.
WIC Special Supplemental Nutrition Program for Women, Infants, and Children Faith et al. (2006)	Fruit juice – BMIz-score	Definition of fruit juices unclear. No response from the authors.
Zutphen Seven Countries Study - Dutch cohort Feskens and Kromhout (1990)	Total sugars – glucose homeostasis	Cross-sectional analysis.

BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FJ, fruit juice; FPG, fasting plasma glucose; HDL-c, high density lipoprotein cholesterol; HTN, hypertension; LDL-c, low density lipoprotein cholesterol; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; SSBs, sugar-sweetened beverages; T2DM, type 2 diabetes mellitus; TG, triglycerides; WC, waist circumference.



3. Observational studies on dental caries

Cohort, publication	Exposure-endpoint excluded	Reasons for exclusion
BTT Birth-to-Ten Study MacKeown et al. (2000)	Added sugars – dmfs	Insufficient data available in the publication for a scientific assessment: unclear data analysis for the longitudinal sample; intake of added sugars and caries incidence reported for the whole sample and not per quartiles, as apparently analysed. No response from the authors.
Campain et al. (2003)	Total sugars – DFS/DMFS/caries increment	Insufficient data available in the publication for a scientific assessment: results only reported for categories of food with "high", "medium" or "low" sugars and starch content, but quantitative sugar intakes are not reported in the publication or used as independent variable in the analyses. No response from the authors.
DDHP Detroit Dental Health Project Lim et al. (2008)	SSBs/FJs – caries increment	Beverages analysed by clusters, which are based on the proportion of consumption of beverages for each individual and change in time. We asked individual data but did not get it. The data available can't be used in the assessment. Total sugars only a variable used for adjustment: even if caries incidence presented by tertiles, this was not the objective of the analysis (non-adjusted values).
Pelotas Peres et al. (2016)	Total sugars – dmft/DMFT	The paper does not report a quantitative level of sugars intake (in g/d). Individual data received from the authors but could not be used. Subjects were stratified into groups of sugar intake, but the amount of sugar intake was not reported.
Rodrigues et al. (1999) Rodrigues and Sheiham (2000)	Total sugars – caries increment	The papers do not report on sugar intake (in g/day) for each participant neither on the one-year DMFT increment for each participant. No response from the authors.
Stecksen-Blicks and Gustafsson (1986)	Total sugars/sucrose – caries increment	The paper does not analyse sucrose and total sugars as independent variables on caries endpoints. Additional data that was requested from authors was destroyed and authors provided a publication that did not contain the needed information. Individual data for reanalysis does not exist.

DMFS: decayed, missing, filled surfaces; DMFT: decayed, missing, filled teeth; DFS: decayed, filled surfaces; FJ: fruit juice; SSBs: sugar-sweetened beverages.



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